

LA CRONICIZZAZIONE

Se, quando e perché

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Sistema Socio Sanitario



Regione
Lombardia
ASST Gaetano Pini



State of the Art Safety Standards in RA
THE EUROPEAN SOCIETY OF REGIONAL
ANAESTHESIA & PAIN THERAPY



European Society of
Regional Anaesthesia
& Pain Therapy

ESRA ITALIA

DEFINITION OF PAIN

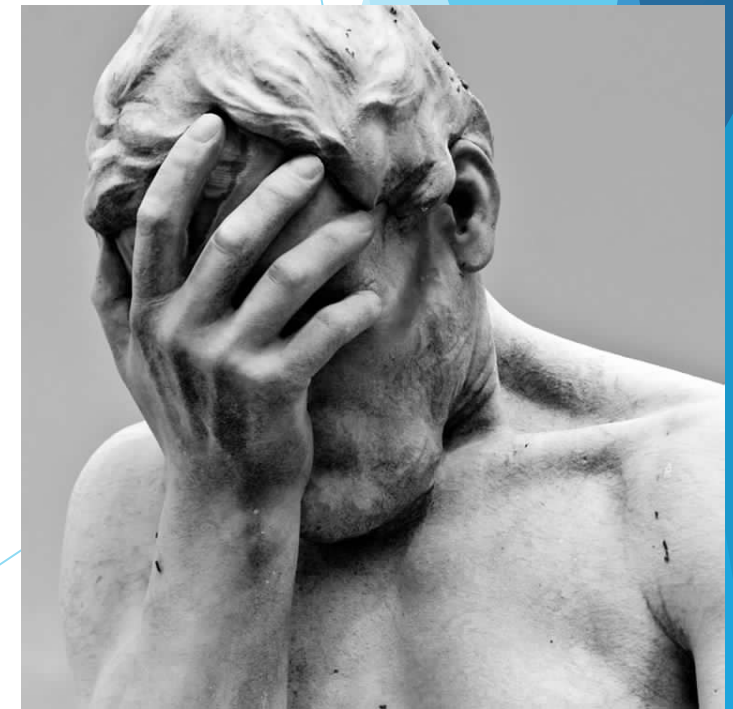
IASP DEFINITION

«Unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage»

TWO COMPONENTS

1. PERCEPTIVE (nociception)

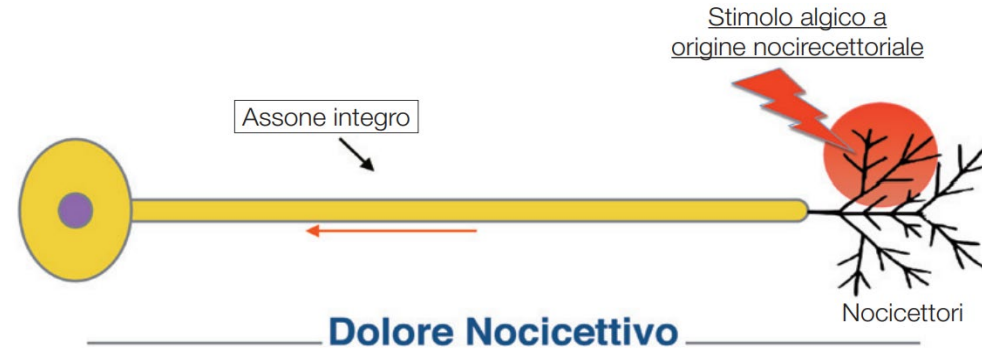
2. PROCESSING
(experience of pain)



DEFINITIONS OF PAIN

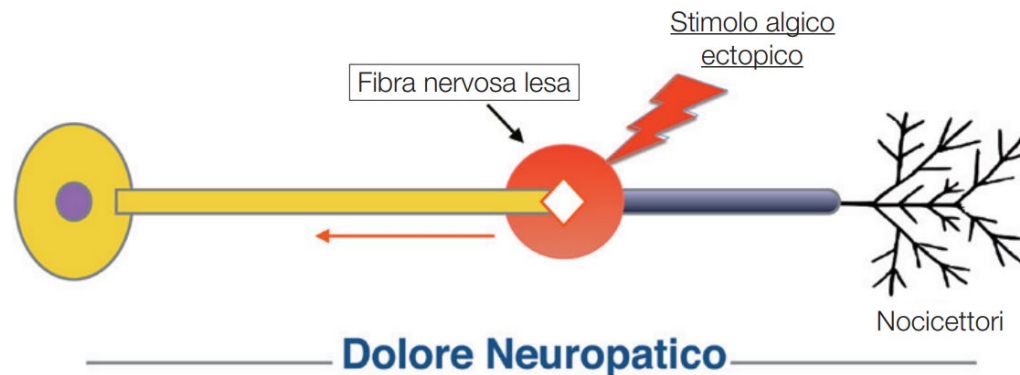
NOCICEPTIVE PAIN

Determined by actual/potential damage to NON-neural tissue, due to activation of nociceptors



NEUROPATHIC PAIN

Causato da una lesione/malattia del sistema somatosensoriale. Può essere centrale o periferico



NOCIPLASTIC PAIN

Altered nociception without evidence of actual/potential tissue damage or disease/lesion of the somatosensory system

NOCICEPTIVE PAIN

IASP DEFINITION

Actual/potential damage to NON-neurological tissue and which is due to the activation of nociceptors

CHARACTERISTICS

- Frequent
- Symptomatic + causal
- Inflammatory/Structural mechanics
- NSAIDs, paracetamol and opioids
- Local distribution
- Variable intensity

Nociceptive

Causes

Somatic

- Bones (bone fracture, metastases)
- Muscles (dystonia, muscle spasm)
- Joints (osteoarthritis)
- Skin (postoperative pain, burns)

Visceral

- Mucosal injury (peptic ulcer)
- Obstruction or capsular distension (gallstones, kidney stones)
- Ischaemia (angina, mesenteric ischaemia)
- Tissue injury (cancer, cirrhosis)

Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *Lancet*. 2021 May 29;397(10289):2082-2097. doi: 10.1016/S0140-6736(21)00393-7. PMID: 34062143

NEUROPATHIC PAIN

IASP DEFINITION

Injury or disease of the somatosensory system

CHARACTERISTICS

- Lesion somato-sensory system
- Paresthesia
- Metameric distribution/innervated region
- Regional hypotrophy
- Hypo/anesthesia
- NOT variable intensity



NB: High prevalence and ↓↓↓ quality of life

Umberto Tarantino (foto) Lorenzo Romano Eleonora Piccirilli Dipartimento di Ortopedia e Traumatologia, Università Tor Vergata, Fondazione Policlinico Tor Vergata; *Giornale Italiano di Ortopedia e Traumatologia* 2015;41:165-172

Causes

Central

- Traumatic (spinal cord injury)
- Vascular (stroke)
- Neurodegenerative (Parkinson's disease)
- Autoimmune (multiple sclerosis)
- Inflammatory (transverse myelitis)

Peripheral

- Infections (HIV, acute herpes zoster or postherpetic neuralgia)
- Nerve compression (carpal tunnel syndrome)
- Trauma (complex regional pain syndrome type 2)
- Metabolic (amyloidosis, nutritional deficiencies)
- Ischaemic (peripheral vascular disease, diabetes)
- Toxic (chemotherapy-induced peripheral neuropathy)
- Auto-immune (Guillain-Barré syndrome)
- Genetic (inherited neuropathy)

Spinal cord injury



Stroke



Postherpetic neuralgia



Peripheral vascular disease, diabetes



Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *Lancet*. 2021 May 29;397(10289):2082-2097. doi: 10.1016/S0140-6736(21)00393-7. PMID: 34062143

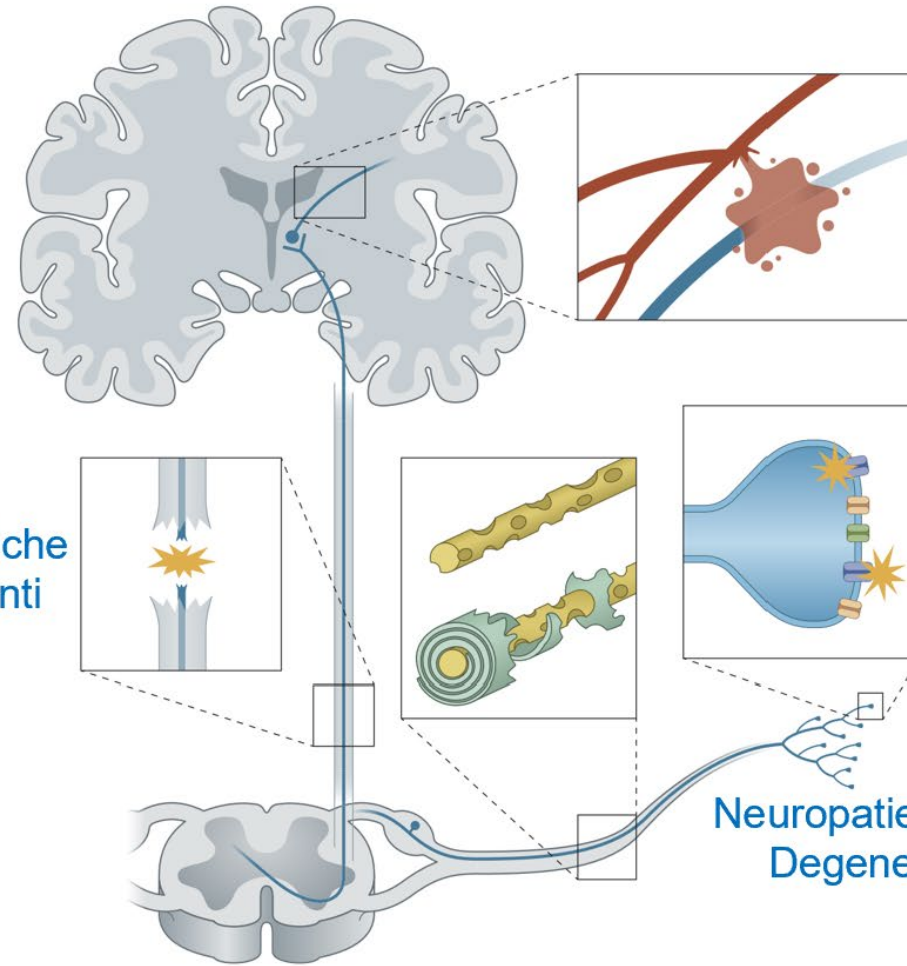
NEUROPATHIC PAIN

Examples of injury > neuropathic pain

Neuropathic pain (DN)

Pain that arises as a direct consequence of a lesion or pathology affecting the somatosensory system at a peripheral or central level

Lesioni traumatiche
o demielinizzanti



Stroke o lesioni
demyelinizzanti

Mutazioni geniche

Neuropatie demielinizzanti o
Degenerativo-assonali

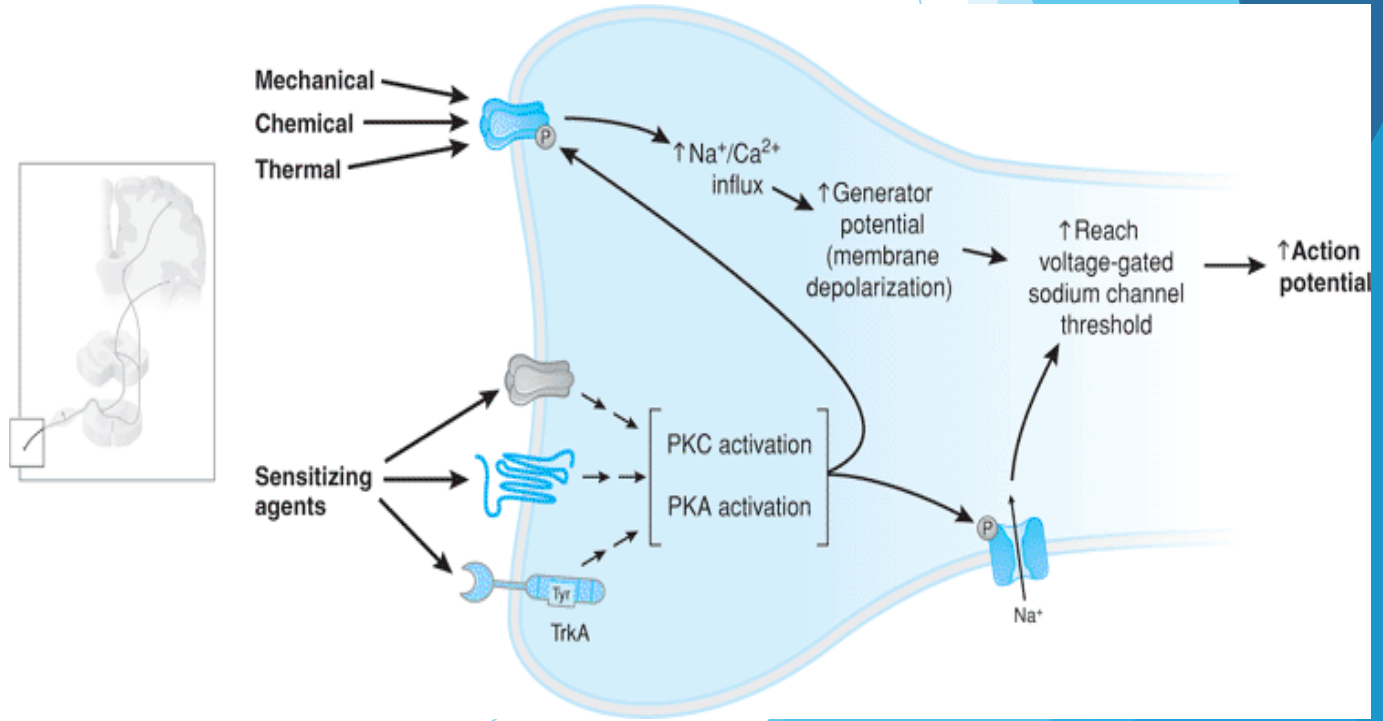
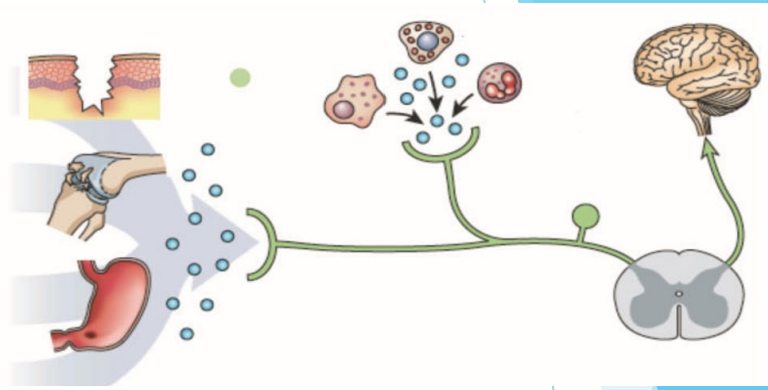
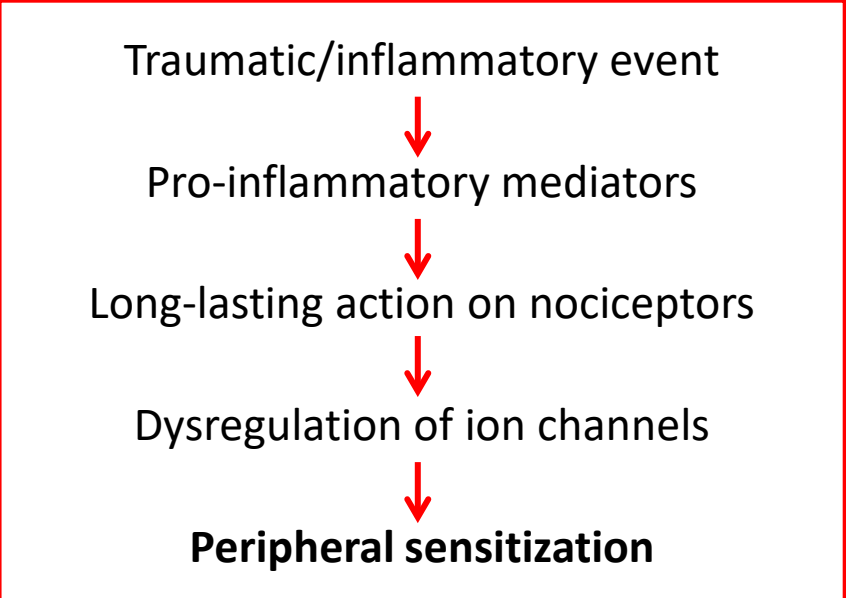
NB [Finnerup et al. Physiol Rev 2021](#)

NEUROPATHIC PAIN: peripheral sensitization

- Inflammatory pain
- Inflammatory infiltrate = **sensitizing agents**
 - bind nociceptor receptors
 - Alteration of pain threshold



Harmless stimuli cause pain
Presence of pain in absence of stimuli



NEUROPATHIC PAIN

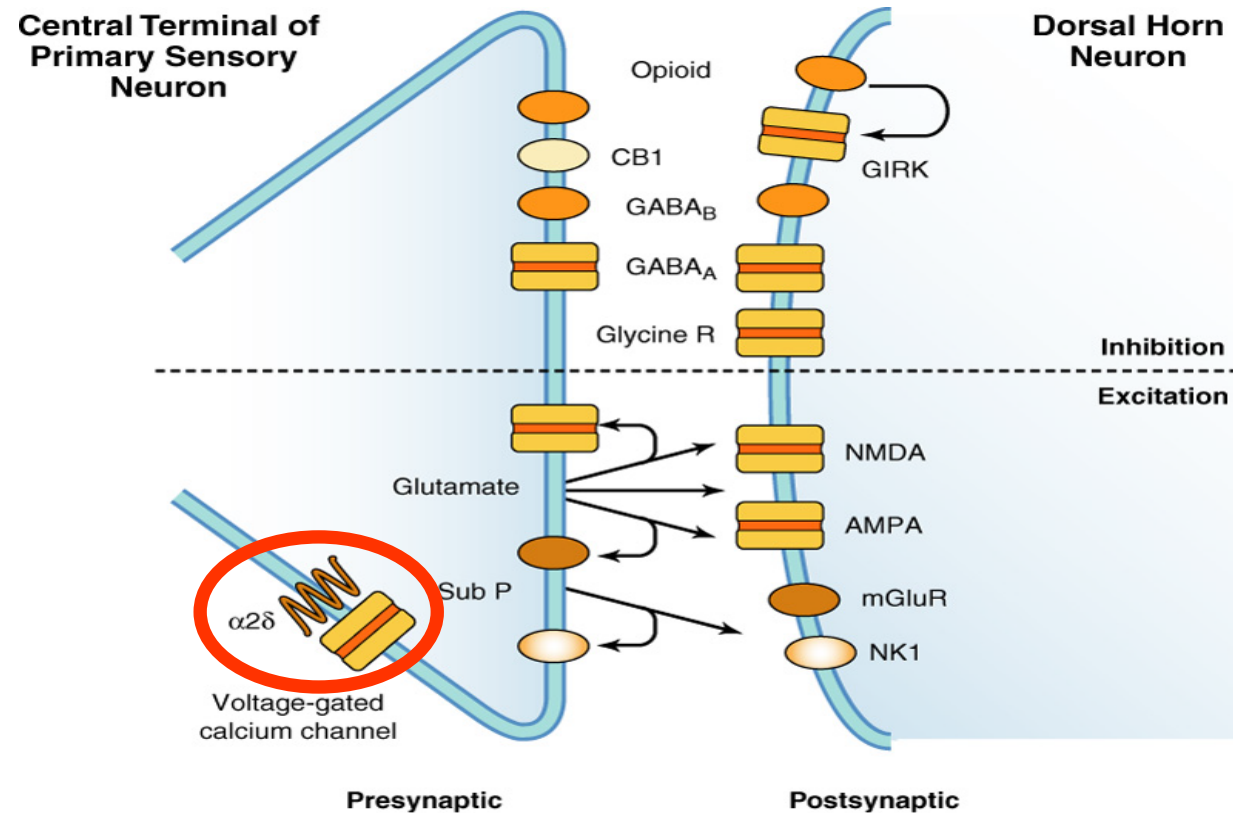
Physiologically:

Opening Ca channels → neurotransmitter release

Peripheral neuron injury → ↑↑↑ voltage-gated calcium channels (up to 10 times)

→ **Abnormal transmission at the spinal level**

↑
**Increased expression
approximately 10-fold**
□



NEUROPATHIC PAIN: central sensitization

Aumento dell'attività afferente
(di origine nocicettiva o neuropatica)

Eccessiva depolarizzazione

Attivazione canali Ca^{++} e NMDA

Neurotossicità indotta da aminoacidi
eccitatori e ingresso Ca^{++}

modificazioni della memoria cellulare
(*C-fos*, *mRNA*)

Modificazione dei contatti sinaptici

DOLORE PERSISTENTE

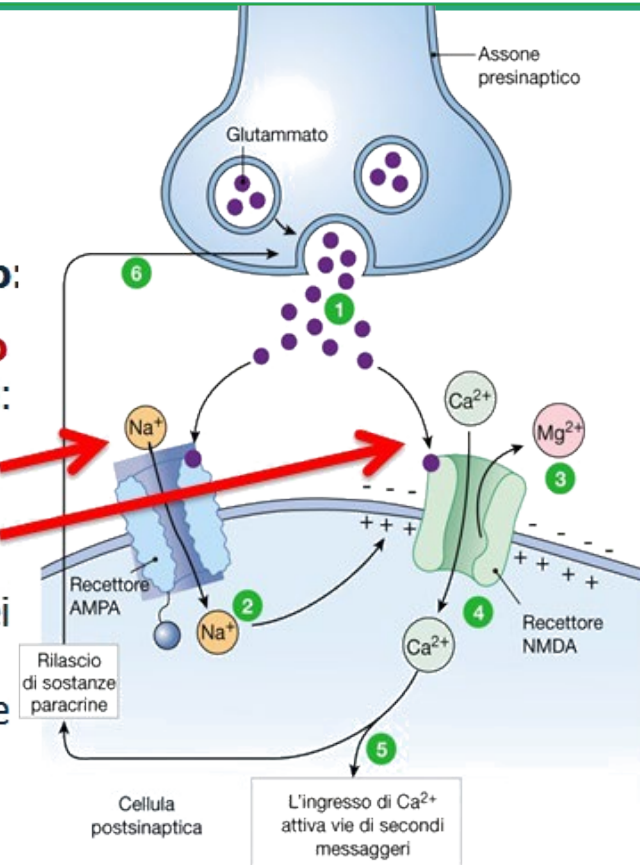
**Neurone
post-sinaptico:**

Il **glutammato**
attiva i recettori:

AMPA (Na^+)

NMDA (Ca^{++})

con apertura dei
canali e nuova
depolarizzazione



1 Viene rilasciato glutammato.

2 L'ingresso netto di Na^+
depolarizza la cellula postsinaptica.

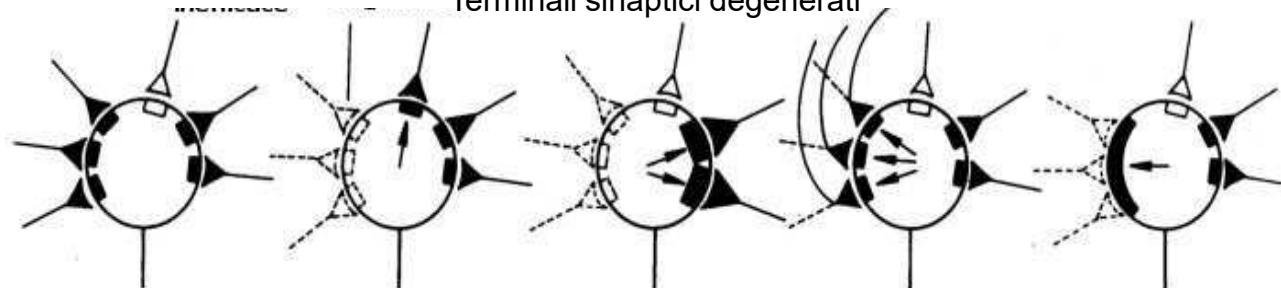
3 La depolarizzazione allontana
gli ioni Mg^{2+} e apre il canale.

4 Entra Ca^{2+} nel citoplasma.

5 La cellula diventa più sensibile
al glutammato.

6 Sostanze paracrine rilasciate dalla
cellula postsinaptica aumentano
il rilascio di glutammato da parte
della cellula presinaptica.

Terminali sinaptici degenerati



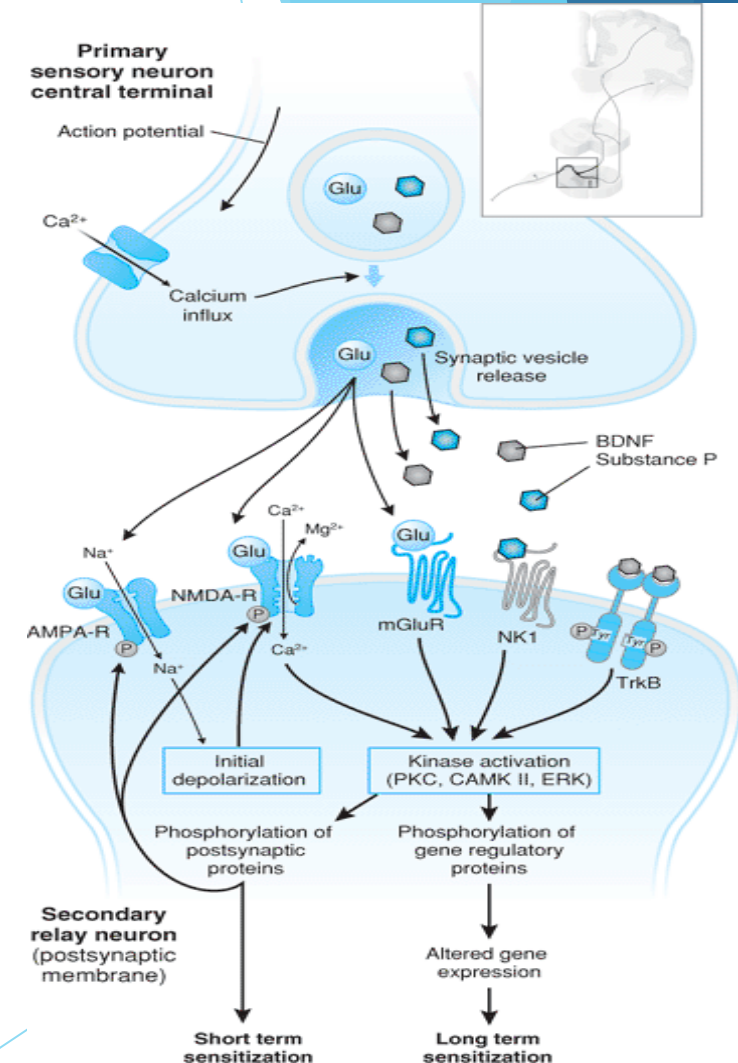
Sinapsi precedentemente inefficaci
divengono attive

Formazione di nuove
connessioni aberranti

**Ipersensibilità
a
neuromodulatori**

SPINAL SENSITIZATION

Primum movens → activation of NMDA receptors due to abnormal stimuli coming from the periphery



MIXED PAIN

Potential mixed pain states

Sciatica, Low back pain, Neck pain, Cancer pain, Osteoarthritis pain, Chronic postsurgical pain, Musculoskeletal disorders, Chronic Temporomandibular disorders, Lumbar spinal stenosis, Pain in Fabry Disease, Chronic joint pain, Painful ankylosing spondylitis, Leprosy, Burning mouth syndrome, ...

Headaches
Vulvodynia
Interstitial cystitis
...

Nociplastic

Fibromyalgia
Irritable bowel
Chronic fatigue
...

Ankylosing spondylitis
Unspecific back pain
Rheumatoid arthritis
Sickle-cell disease
Myofascial pain
Osteoarthritis
Visceral pain
Tendonitis
Bursitis
Gout
...

Nociceptive

Mixed

Pain

Neuropathic

...
Sciatica
Post-stroke
Spinal cord injury
Multiple sclerosis
Trigeminal neuralgia
Postherpetic neuralgia
Small-fiber neuropathies
Painful polyneuropathies

CRONICIZZAZIONE DEL DOLORE

Se non si riesce ad eliminare la
noxa patogena . . .

. . . il dolore nocicettivo **PERSISTE** sino
a diventare **CRONICO**



CHRONIC PAIN DEFINITIONS

ICD-10 GERMAN ADAPTATION

“Chronic pain disorder with somatic and psychological factors”

Nicholas M, Vlaeyen JWS, Rief W, Barke A, Aziz Q, Benoliel R, Cohen M, Evers S, Giamberardino MA, Goebel A, Korwisi B, Perrot S, Svensson P, Wang SJ, Treede RD; IASP Taskforce for the Classification of Chronic Pain. The IASP classification of chronic pain for ICD-11: chronic primary pain. *Pain*. 2019 Jan;160(1):28-37. doi: 10.1097/j.pain.0000000000001390. PMID: 30586068.

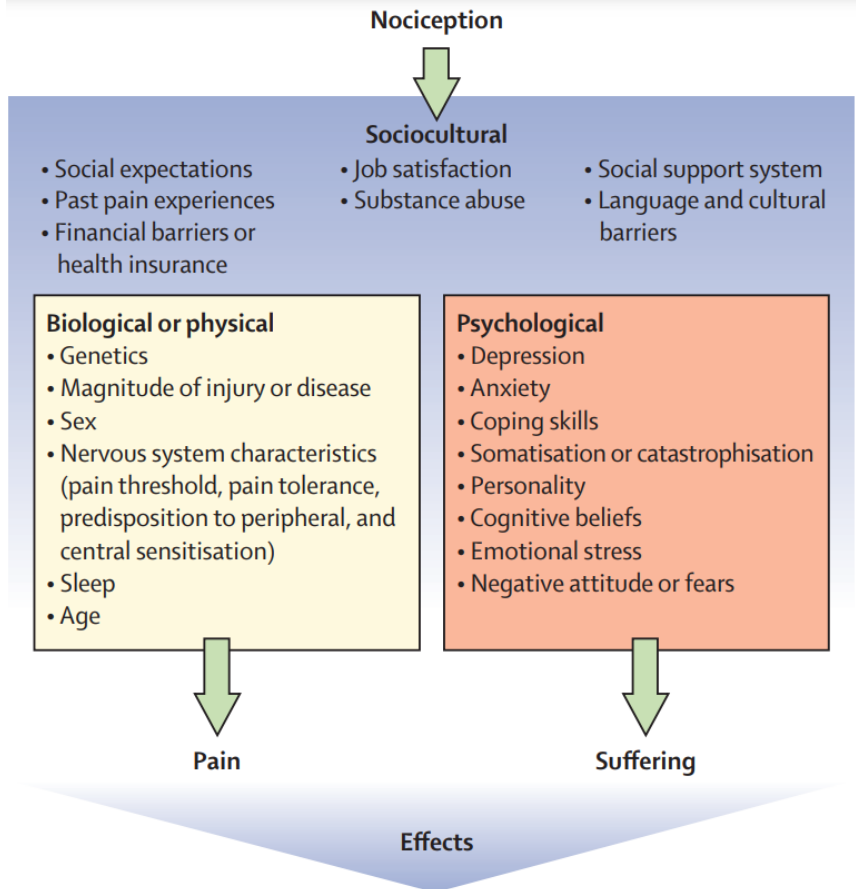
IASP DEFINITION FOR ICD-11

“Chronic pain is pain that lasts or recurs for > 3 months”

Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, Cohen M, Evers S, Finnerup NB, First MB, Giamberardino MA, Kaasa S, Kosek E, Lavand'homme P, Nicholas M, Perrot S, Scholz J, Schug S, Smith BH, Svensson P, Vlaeyen JW, Wang SJ. A classification of chronic pain for ICD-11. *PAIN* 2015;156:1003–7.



Biopsychosocial model and consequences



COMPLEX INTERACTION BETWEEN

- Chronic pain
- Biological factors
- Psychological factors
- Social factors



- Deconditioning
- Biomechanical problems
- Loss of grey matter
- Altered nociceptive pathways
- Medication use or abuse



- Depression
- Cognitive impairment
- Learned helplessness
- Anxiety
- Poor concentration



- Social withdrawal
- Dysfunctional relationships
- Isolation
- Increased suicide risk

Consequences of chronic pain

Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. *Lancet*. 2021 May 29;397(10289):2082-2097. doi: 10.1016/S0140-6736(21)00393-7. PMID: 34062143

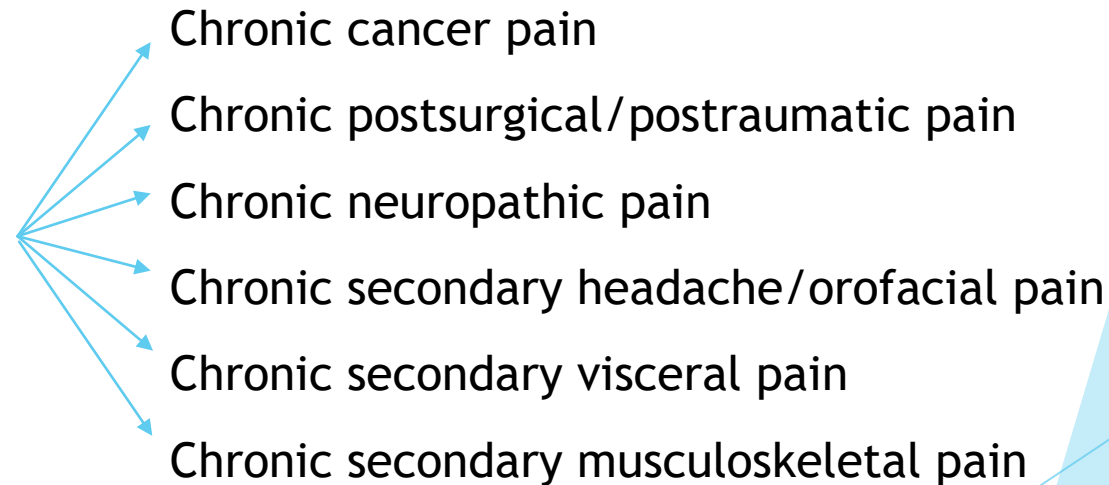
IASP CLASSIFICATION for ICD-11

Chronic primary pain

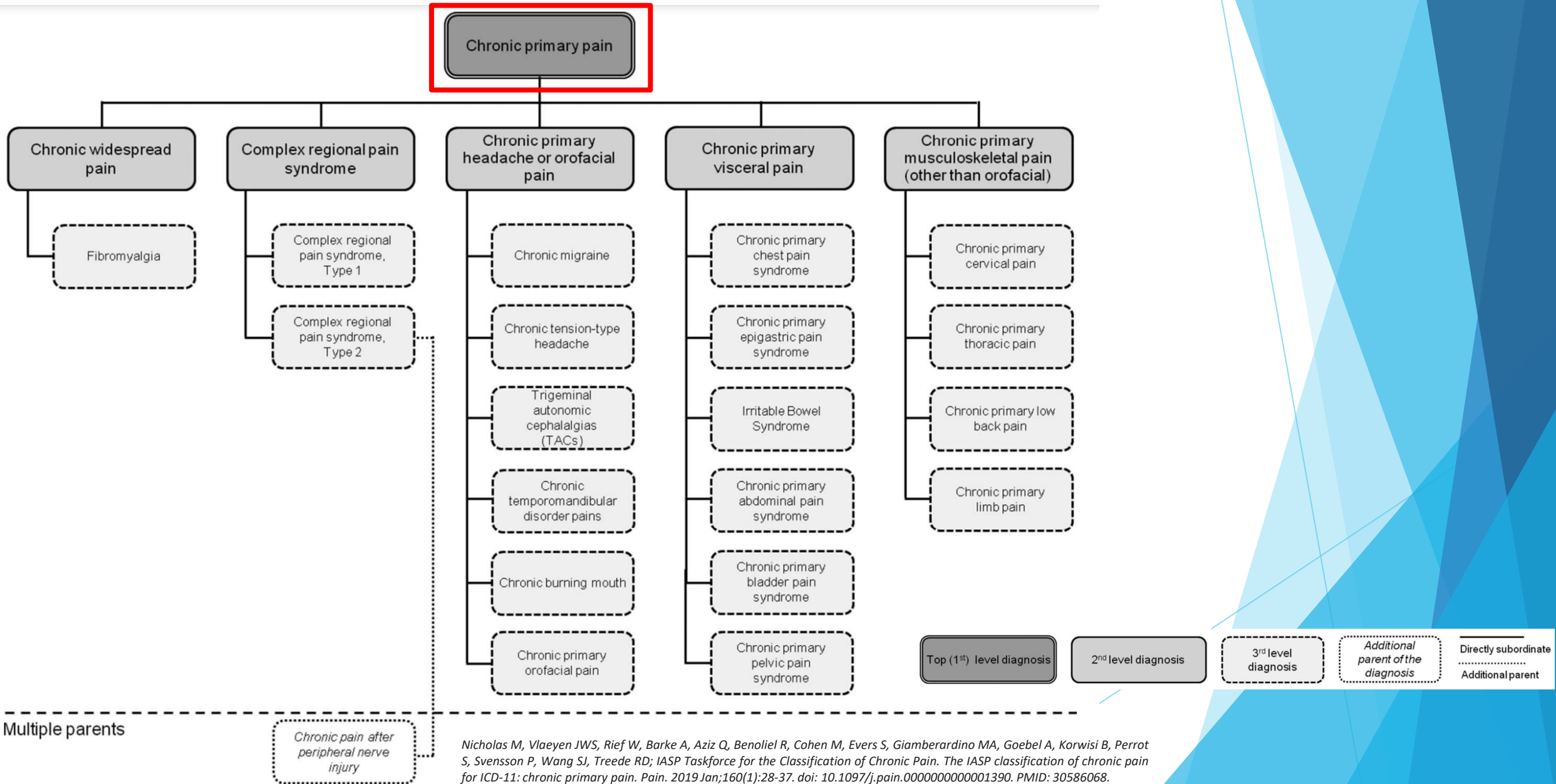
- 1/+ anatomical regions
- Persists/recurs > 3 months
- Emotional distress ± functional disability
- Another diagnosis missing

Secondary pain syndromes

Another diagnosis better accounts for the chronic pain presentation



IASP CLASSIFICATION for ICD-11



Nicholas M, Vlaeyen JWS, Rief W, Barke A, Aziz Q, Benoliel R, Cohen M, Evers S, Giamberardino MA, Goebel A, Korwisi B, Perrot S, Svensson P, Wang SJ, Treede RD; IASP Taskforce for the Classification of Chronic Pain. The IASP classification of chronic pain for ICD-11: chronic primary pain. *Pain*. 2019 Jan;160(1):28-37. doi: 10.1097/j.pain.0000000000001390. PMID: 30586068.

CHRONIC POSTSURGUCAL PAIN

Risk factors

Demographics and lifestyle

- Age
- Gender
- Marital status or living arrangements
- Education level
- Employment status
- Compensation status
- Obesity
- Smoking

Genetic

- Candidate gene mutations associated with increased pain (eg, *COMT*, *OPRM1*, and *GCH1*)

Clinical

- Surgical factors, including surgical technique (open vs laparoscopic), duration of surgery, type of anaesthesia (general vs regional), and perioperative
- Analgesic regimen (systemic vs spinal and pre-emptive); surgical complications and re-operating
- Medical comorbidities
- Previous disability or pain interference

Preoperative pain (area of operation or elsewhere)

Postoperative pain (intensity and duration)

Psychological

- Fear or anxiety
- Depression
- Pain catastrophising
- Other psychological issues (eg, vulnerability factors)

COMT=catechol-o-methyltransferase. *OPRM1*=opioid receptor mu 1.
GCH1=guanosine-5'-triphosphate cyclohydrolase 1.

Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. Lancet. 2019 Apr 13;393(10180):1537-1546. doi: 10.1016/S0140-6736(19)30352-6. PMID: 30983589.

CHRONIC POSTSURGICAL PAIN

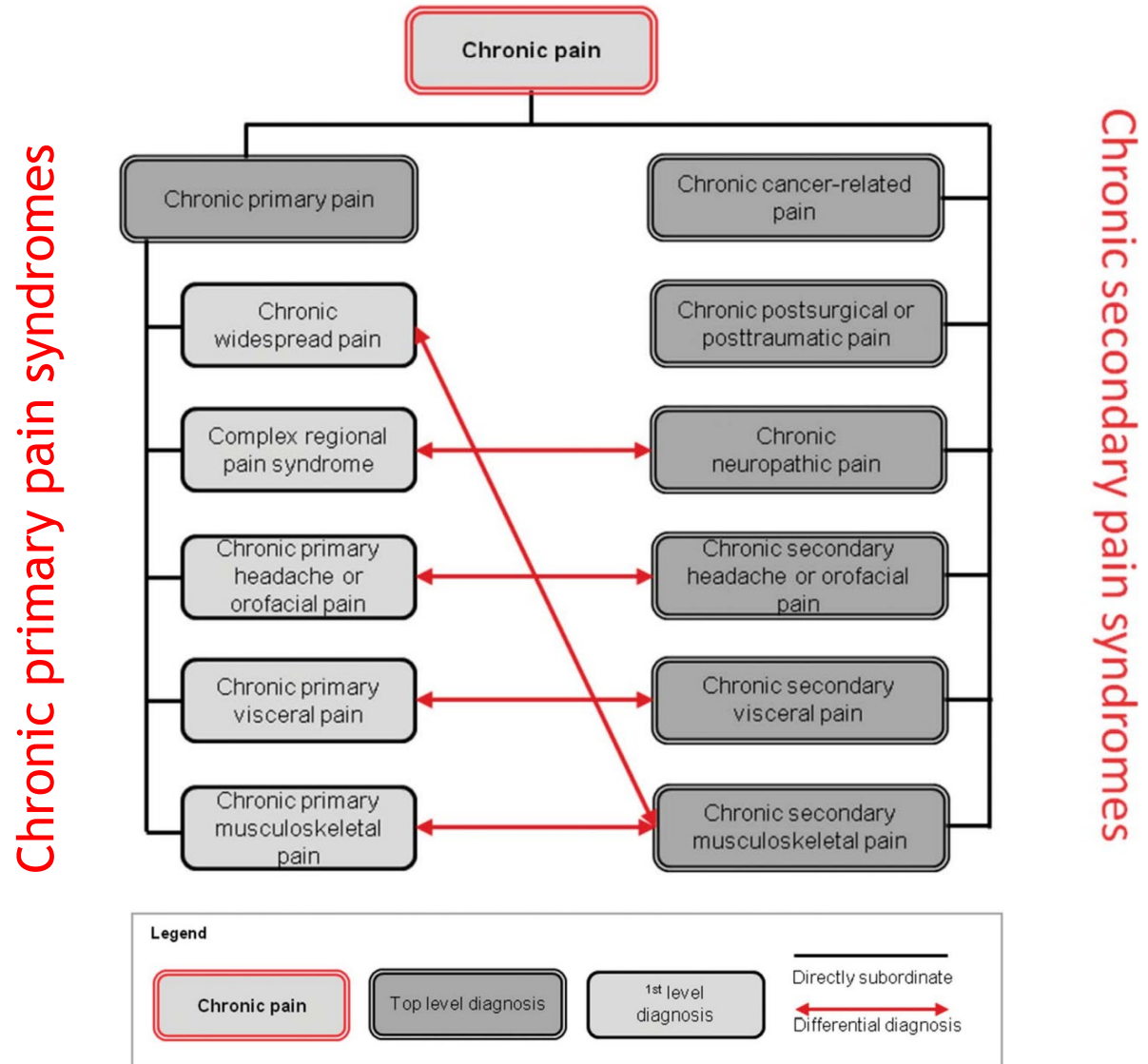
Prevalence	Any intensity (%)	Moderate-severe intensity (%)	Prevalence (%); prevalence if restricted to a severe pain rating	Number of operations in US non-federal community hospitals* in 2014 ⁷
Amputation of limb	30–85%	5–10%	Up to 85% ⁸	Not available
Arthroplasty, knee	13–44%	15%	44% (15%) ⁹	723 086
Caesarean section	6–55%	5–10%	Up to 12% ¹⁰	1 142 680
Cholecystectomy	3–50% ¹¹	Not reported	Not reported	300 245
Craniotomy	0–65% ¹²	25%	12–16% ¹³	Not available
Hip replacement	27%	6%	27% (15%) ⁹	487 625
Inguinal hernia repair	5–63%	2–4%	6–29% ¹⁴	Not available
Laminectomy and spinal fusion	10–40%	4–6% ¹⁵	5–36% ^{16,17}	564 911
Mastectomy	11–57%	5–10%	22% ¹⁸	Not available
Coronary artery bypass graft	30–50%	5–10%	28% (4%) ¹⁹	160 240
Thoracotomy	5–65%	10%	48% ^{20,21}	Not available

*Non-federal community hospitals account for 786 874 (87%) of 902 202 hospital beds in the USA.

Table 1: Prevalence of chronic postsurgical pain in common surgeries in the USA^{11,22–24}

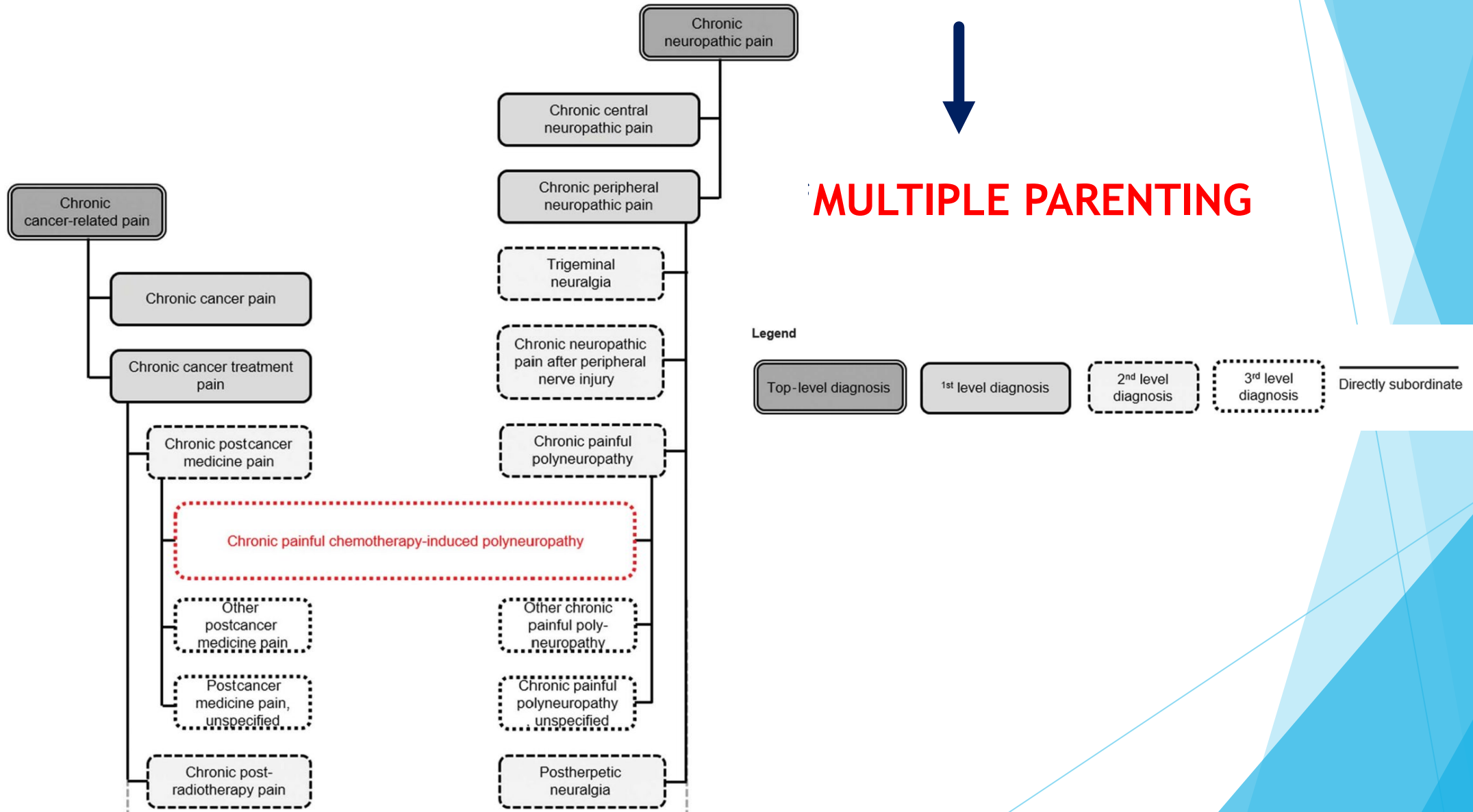
Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. *Lancet*. 2019 Apr 13;393(10180):1537-1546. doi: 10.1016/S0140-6736(19)30352-6. PMID: 30983589.

IASP CLASSIFICATION for ICD-11



IASP CLASSIFICATION for ICD-11

Allows for any given disease (“child”) to belong to more than one section (“parent”)



AVOID CHRONICIZATION

Dolore indipendente dallo stimolo nocicettivo



AUTOMANTENIMENTO



Evitare sensibilizzazione centrale



INTERVENIRE PRECOCEMENTE SUL DOLORE

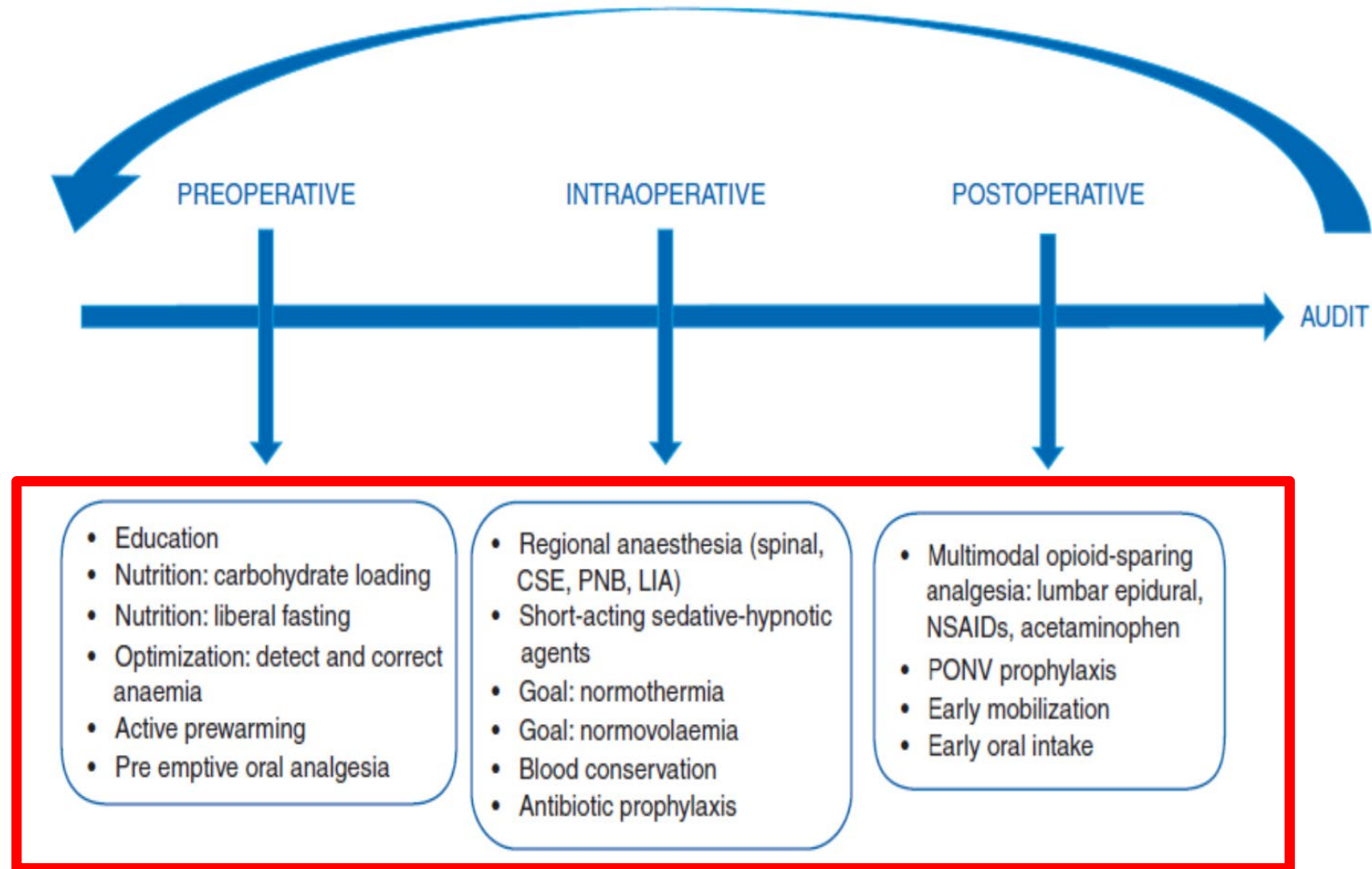
HOW TO PREVENT

L'attesa è cattiva consigliera ...

Table 3. Summary of recommended interventions for the perioperative care of hip and knee replacement

Number	Item	Recommendation	Evidence level	Recommendation grade
1	Preoperative information, education and counseling	Patients should routinely receive preoperative education	Low	Strong
2	Preoperative optimization	4 weeks' or more smoking cessation is recommended prior to surgery	Smoking: High	Strong
		Alcohol cessation programs are recommended for alcohol abusers	Alcohol: Low	Strong
		Anemia should be actively identified, investigated, and corrected preoperatively	High	Strong
3	Preoperative fasting	Clear fluids should be allowed up to 2 h and solids up to 6 h hours prior to induction of anesthesia	Moderate	Strong
4	Standard anesthetic protocol	General anesthesia and neuraxial techniques may both be used as part of multimodal anesthetic regimes	General anesthesia: moderate neuraxial techniques: Moderate	Strong

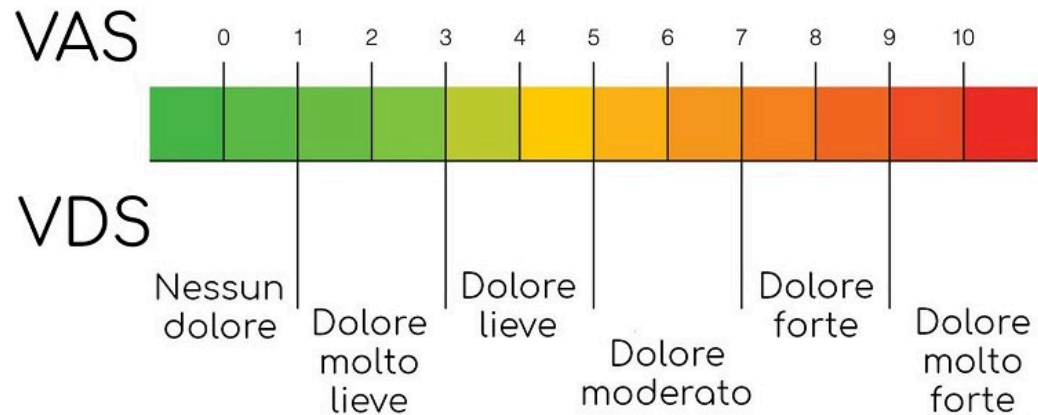
HOW TO PREVENT



HOW TO INTERVENE?

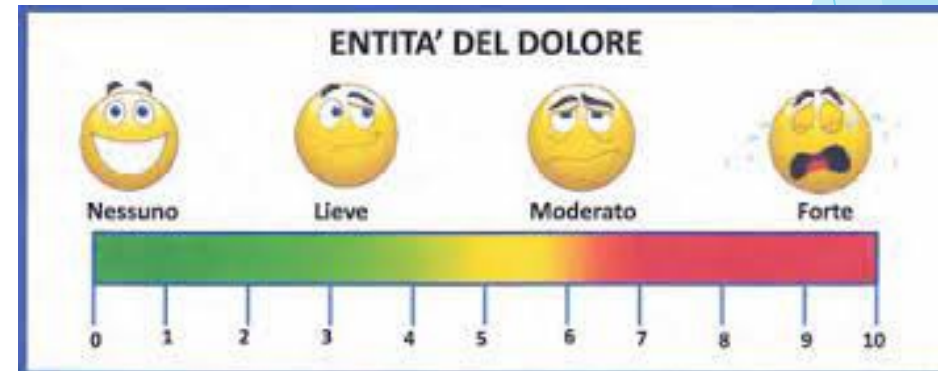
Adeguati strumenti di misura

Scala del dolore



Sistema P.Q.R.S.T.

- P= provocation (fattori favorenti o sfavorenti)
- Q= Quality (come lo definisce, a che cosa assomiglia?)
- R= Radiation (sede)
- S= Severity (intensità cioè quanto è forte)
- T= Time (quando insorge il dolore).



WHAT TO DO

COMUNICAZIONE
CON IL PAZIENTE

TEMPI GIUSTI

LAVORO DI
SQUADRA

Observational Study | J Arthroplasty. 2019 Jul;34(7S):S209-S214.
doi: 10.1016/j.arth.2018.12.038. Epub 2019 Jan 6.

Modifying Patient Expectations Can Enhance Total Hip Arthroplasty Postoperative Satisfaction

Jorge A Padilla¹, James E Feng¹, Afshin A Anoushiravani², William J Hozack³,
Ran Schwarzkopf¹, William B Macaulay¹

Affiliations + expand
PMID: 30795937 DOI: 10.1016/j.arth.2018.12.038

Abstract

Background: A better understanding of patient expectations within the perioperative setting will enable clinicians to better tailor care to the needs of the total hip arthroplasty (THA) recipient. Such an approach will promote patient-centered decision-making and optimize recovery times while enhancing mandated hospital quality metrics. In the present study, we preoperatively and postoperatively surveyed THA candidates to elucidate the relationship between patient expectations and length of stay (LOS).

Methods: This is a multi-institutional prospective study among THA candidates. Patients were surveyed regarding discharge planning 1 week preoperatively and postoperatively to capture perioperative patient expectations and correlate with inpatient LOS.

Results: In total, 93 THAs performed by 6 high-volume orthopedic surgeons at 2 medical centers. Our results demonstrated that patients of male gender and commercial insurance had significantly ($P < .05$) shorter LOS. Shorter LOS patients demonstrated significantly higher levels of LOS acceptance ("very comfortable" rate in same-day discharge: 75.0% and next-day discharge: 63.8%; 2 days: 40.7%; 3+ days: 42.9%; $P < .05$) and a higher likelihood to participate in SDD programs. Postoperatively, patients with a shorter LOS had more acceptance to their LOS, albeit not statistically significant ($P = .20$).

Conclusion: Our results suggest that guiding patient expectations within the perioperative setting is an essential component for successful and timely discharge after THA. Having clear and transparent discussion with the surgical team regarding the perioperative course can improve a THA candidate's understanding and buy-in with the postoperative plan, regardless of LOS. Finally,



C. E. H. Scott,
D. J. MacDonald,
C. R. Howie

From Royal Infirmary
of Edinburgh,
Edinburgh,
United Kingdom

■ ARTHROPLASTY

'Worse than death' and waiting for a joint arthroplasty

Aims

The EuroQol five-dimension (EQ-5D) questionnaire is a widely used multiattribute general health questionnaire where an EQ-5D < 0 defines a state 'worse than death' (WTD). The aim of this study was to determine the proportion of patients awaiting total hip arthroplasty (THA) or total knee arthroplasty (TKA) in a health state WTD and to identify associations with this state. Secondary aims were to examine the effect of WTD status on one-year outcomes.

Patients and Methods

A cross-sectional analysis of 2073 patients undergoing 2073 THAs (mean age 67.4 years (so 11.6; 14 to 95); mean body mass index (BMI) 28.5 kg/m² (so 5.7; 15 to 72); 1253 female (60%)) and 2168 patients undergoing 2168 TKAs (mean age 69.3 years (so 9.6; 22 to 91); BMI 30.8 kg/m² (so 5.8; 13 to 57); 1244 female (57%)) were recorded. Univariate analysis was used to identify variables associated with an EQ-5D score < 0: age, BMI, sex, deprivation quintile, comorbidities, and joint-specific function measured using the Oxford Hip Score (OHS) or Oxford Knee Score (OKS). Multivariate logistic regression was performed. EQ-5D and OHS/OKS were repeated one year following surgery in 1555 THAs and 1700 TKAs.

Results

Preoperatively, 391 THA patients (19%) and 263 TKA patients (12%) were WTD. Multivariate analysis identified preoperative OHS, deprivation, and chronic obstructive pulmonary disease in THA, and OKS, peripheral arterial disease, and inflammatory arthropathy in TKA as independently associated with WTD status ($p < 0.05$). One year following arthroplasty EQ-5D scores improved significantly ($p < 0.001$) and WTD rates reduced to 35 (2%) following THA and 53 (3%) following TKA. Patients who were WTD preoperatively achieved significantly ($p < 0.001$) worse joint-specific Oxford scores and satisfaction rates one year following joint arthroplasty, compared with those not WTD preoperatively.

Conclusion

In total, 19% of patients awaiting THA and 12% awaiting TKA for degenerative joint disease are in a health state WTD. Although specific comorbidities contribute to this, hip- or knee-specific function, mainly pain, appear key determinants and can be reliably reversed with an arthroplasty.

Cite this article: *Bone Joint J* 2019;101-B:941-950.

In modern society, there is increasing demand for healthcare interventions to be economically viable and cost-effective. To quantify this, the number of quality-adjusted life-years (QALYs) delivered by the intervention is calculated, based on the Euro-

representing full health and 0 death.¹ Negative scores define, therefore, a state 'worse than death' (WTD). Of the 243 possible health states, 84 have negative utility scores and hence are deemed WTD. The ability to score health states WTD

> Acad Med. 2013 May;88(5):585-92. doi: 10.1097/ACM.0b013e31828b0289.

There is no "i" in teamwork in the patient-centered medical home: defining teamwork competencies for academic practice

Emily L Leasure¹, Ronald R Jones, Lauren B Meade, Marla I Sanger, Kris G Thomas, Virginia P Tilden, Judith L Bowen, Eric J Warm

Affiliations + expand
PMID: 23524923 DOI: 10.1097/ACM.0b013e31828b0289

Abstract

Evidence suggests that teamwork is essential for safe, reliable practice. Creating health care teams able to function effectively in patient-centered medical homes (PCMHs), practices that organize care around the patient and demonstrate achievement of defined quality care standards, remains challenging. Preparing trainees for practice in interprofessional teams is particularly challenging in academic health centers where health professions curricula are largely siloed. Here, the authors review a well-delineated set of teamwork competencies that are important for high-functioning teams and suggest how these competencies might be useful for interprofessional team training and achievement of PCMH standards. The five competencies are (1) team leadership, the ability to coordinate team members' activities, ensure appropriate task distribution, evaluate effectiveness, and inspire high-level performance, (2) mutual performance monitoring, the ability to develop a shared understanding among team members regarding intentions, roles, and responsibilities so as to accurately monitor one another's performance for collective success, (3) backup behavior, the ability to anticipate the needs of other team members and shift responsibilities during times of variable workload, (4) adaptability, the capability of team members to adjust their strategy for completing tasks on the basis of feedback from the work environment, and (5) team orientation, the tendency to prioritize team goals over individual goals, encourage alternative perspectives, and show respect and regard for each team member. Relating each competency to a vignette from an academic primary care clinic, the authors describe potential strategies for improving teamwork learning and applying the teamwork competencies to academic PCMH practices.

BEST PRACTICES PAIN MANAGEMENT



**DIAGNOSIS
+
MEASURABLE
OUTCOMES**
(QUALITY OF LIFE)



**PATIENT
CENTRED
APPROACH**



**MULTIDISCIPLINARY
APPROACH**



**LESS INVASIVE
TREATMENTS**
(WEIGHT LOSS, EXERCISE)

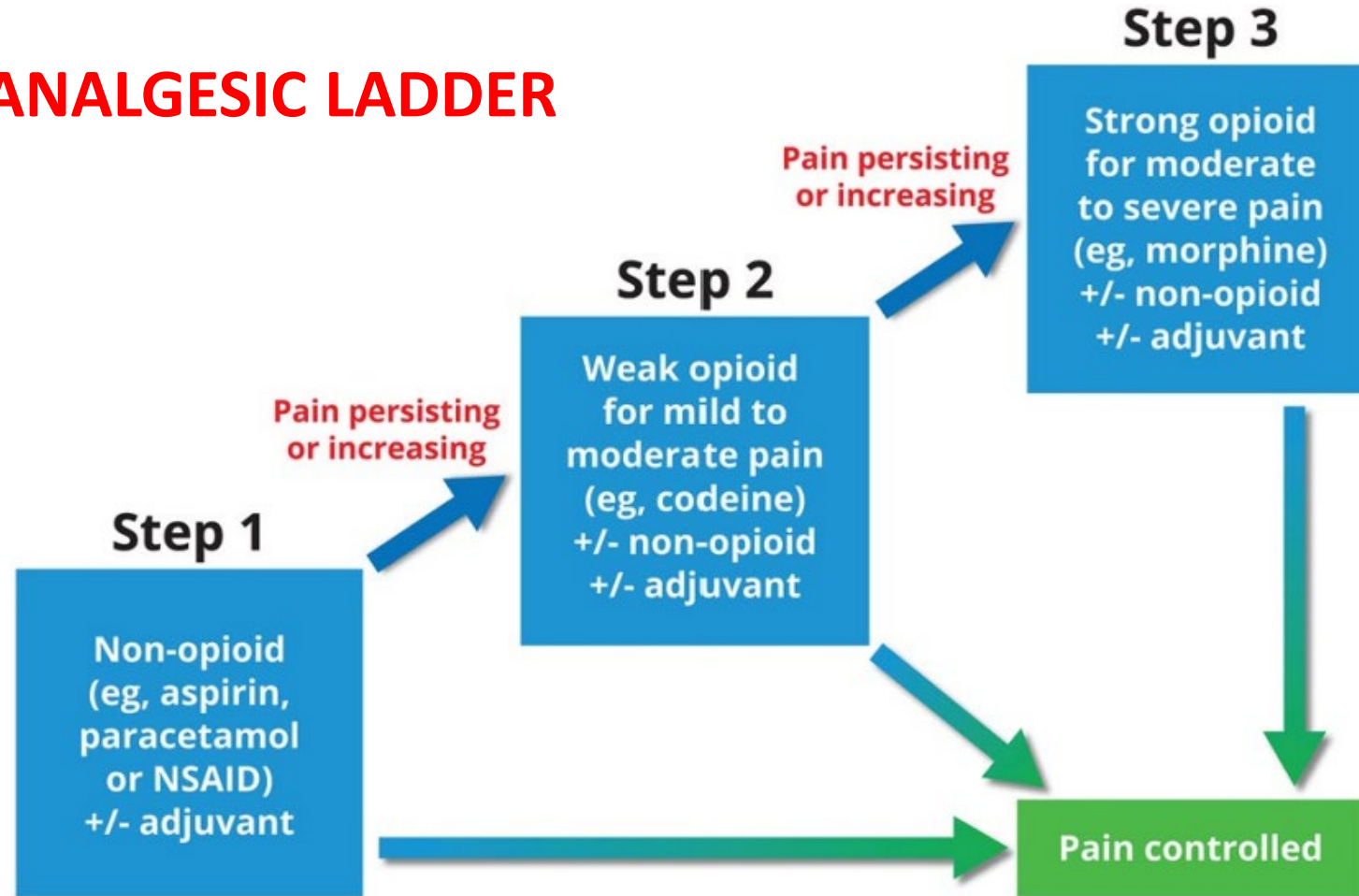


**TREATMENT
TAILORED**























TREATMENT CONSIDERATIONS

WHO ANALGESIC LADDER

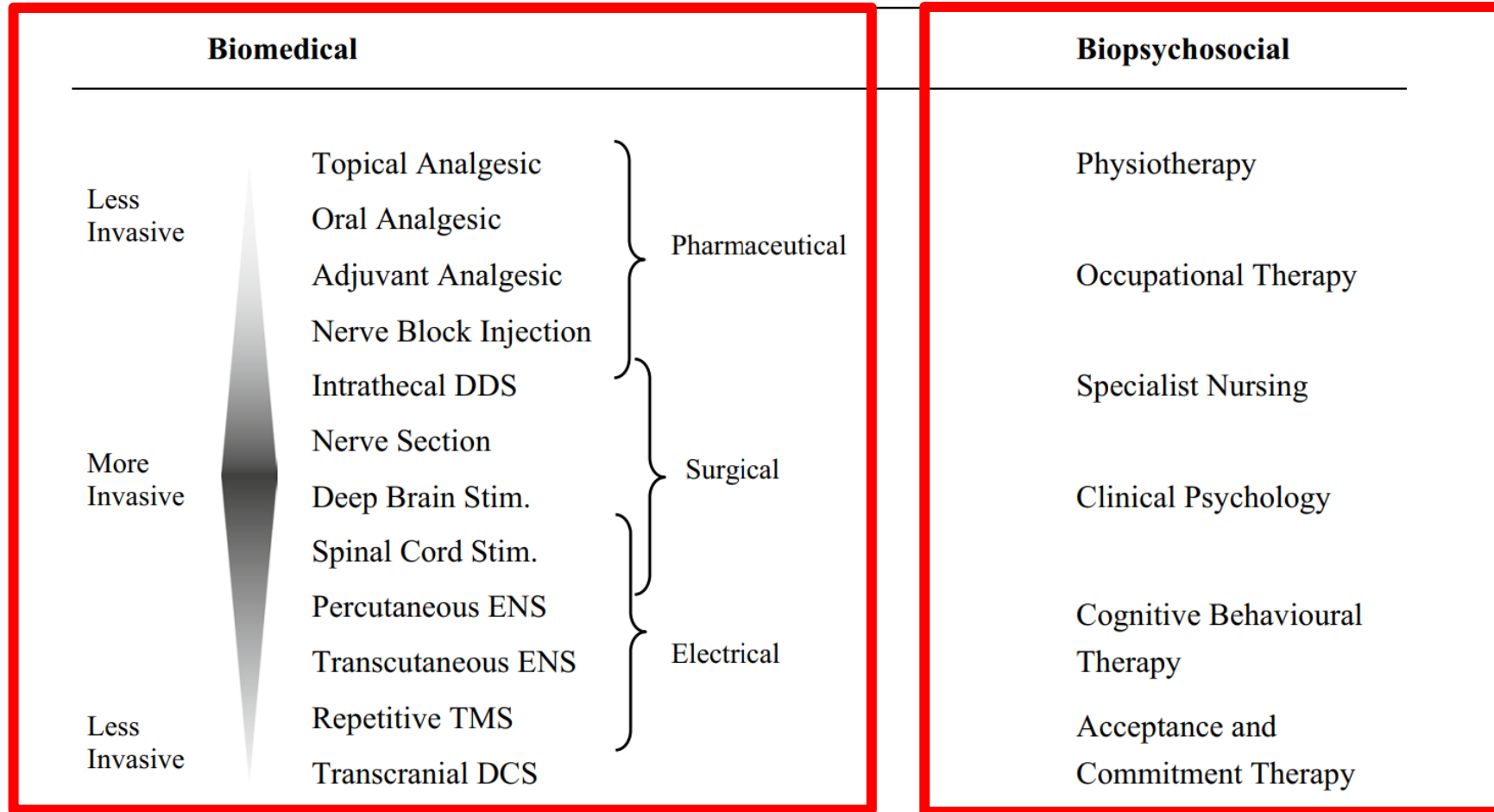


TREATMENT CONSIDERATIONS

-  Nociceptive
-  Neuropathic
-  Nociplastic

-   Anticonvulsants
-    Analgesic antidepressants
-   Image guided injections
-    Behavioural interventions
-   Neuromodulation
-  Non-steroidal anti-inflammatory drugs
-   Opioids
-   Exercise

TREATMENT APPROACHES



DDS drug delivery system, **Stim.** stimulation, **ENS** electrical nerve stimulation, **TMS** transcranial magnetic stimulation, **DCS** direct current stimulation

EAN GUIDELINES - CNT

EAN guidelines on central neurostimulation therapy in chronic pain conditions

Eur J Neurol. 2016 Oct;23(10):1489-99. doi: 10.1111/ene.13103. Epub 2016 Aug 11.

Table 2 Summary of GRADE recommendations for neurostimulation in chronic pain

Procedure	Neuropathic pain	Post-surgical chronic back and leg pain	CRPS I	Fibromyalgia
Spinal cord stimulation				
SCS versus conventional management	Weak for	Weak for	Weak for	
SCS versus reoperation		Weak for		
Deep brain stimulation	Inconclusive			
Epidural motor cortex stimulation	Weak for			
Repetitive transcranial magnetic stimulation				
rTMS of M1	Weak for		Inconclusive	Weak for
rTMS of DLPFC	Inconclusive			Inconclusive
Transcranial direct current stimulation				
tDCS of M1	Weak for (inconclusive in SCI)			Inconclusive
tDCS of DLPFC	Inconclusive			Inconclusive

CRPS I, complex regional pain syndrome type I; DLPFC, dorsolateral prefrontal cortex; M1, primary motor cortex; rTMS, repetitive transcranial magnetic stimulation; SCI, spinal cord injury; SCS, spinal cord stimulation; tDCS, transcranial direct current stimulation.

EAN GUIDLINES - CNT

EAN guidelines on central neurostimulation therapy in chronic pain conditions

Eur J Neurol. 2016 Oct;23(10):1489-99. doi: 10.1111/ene.13103. Epub 2016 Aug 11.

Procedure	Neuropathic pain				Complex regional pain syndrome type I				Fibromyalgia			
	Final quality of evidence	Effect size	Tolerability/safety	Values and preferences	Final quality of evidence	Effect size	Tolerability/safety	Values and preferences	Final quality of evidence	Effect size	Tolerability/safety	Values and preferences
SCS ^a	Low	Low	Moderate	ND	Low	Low	Moderate	ND				
DBS	Very low	Very low	Moderate	ND								
MCS	Very low	Low	Moderate	High ^b								
rTMS of M1	Low	Low	High	ND	Very low	Low	High	ND	Low	Low	High	ND
rTMS of DLPFC	Very low	Low	High	ND					Very low	Low	High	ND
tDCS of M1	Low	Low	High	ND					Low	Low	High	ND
tDCS of DLPFC	Very low	Low	High	ND					Very low	Low	High	ND

VI RINGRAZIO PER L'ATTENZIONE

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Centro Specialistico Ortopedico Traumatologico
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